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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/654,227	08/31/2000	Juergen Hilman	PLOVIN-1-A	5622

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EXAMINER
BAHAR, MOJDEH

ART UNIT	PAPER NUMBER
1617	13

DATE MAILED: 05/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N . 09/654,227	Applicant(s) HEIL ET AL.	
	Examiner Mojdeh Bahar	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7,9-14,16-19,21,22 and 36-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7,9-14,16-19,21,22 and 36-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response and remarks to the first office action of September 13, 2001, submitted February 8, 2002 are acknowledged. Examiner also notes the informal admission of supplemental data (i.e., the data is not submitted in declaration form). Applicant's amendment and remarks are persuasive to remove the objections and the rejections under 35 USC 112, second paragraph and 35 USC 102.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-7, 9-14, 16-17 and 36-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gast (WO 98/04269).

Gast (WO 98/04269) teaches a combination composition comprising 250 microgram to 4 mg of drospirenone and 10-20 microgram of ethinyl estrsdiol, and pharmaceutically acceptable carriers and excipients, see page 9, lines 19-33 and claim 1. Gast (WO 98/04269) also teaches a contraceptive kit adapted for daily oral administration which comprises 28 separate dosage units with 3-5 dosage units being a non-contraceptive placebo, see page 10, lines 15-24 in particular.

Gast (WO 98/04269) does not teach drospirenone or ethinyl estradiol in micronized form, neither does it explicitly teach the release time of the actives or a kit containing 28 dosage units all containing drospirenone and ethinyl estrsdiol. Gast does not particularly teach the employment of esters or prodrugs of the actives herein.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ drospirenone or ethinyl estradiol in micronized form. It would have also been obvious to include 28 dosage units all containing drospirenone and ethinyl estrsdiol in Gast's kit. It would have also been obvious to employ esters and prodrugs of the actives herein in a composition and a kit.

One of ordinary skill in the art would have been motivated to employ known pharmaceutical actives in micronized form because variations or optimizations of the dosage regimen of compounds well known to be administered together in combination, are considered within the skill of the artisan. Note that the Skilled Artisan would be motivated to employ esters and prodrugs of known actives because they are reasonably expected to possess the same physiological and pharmacological activities.

Claims 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gast (WO 98/04267).

Gast (WO 98/04267) discloses a combination composition and pharmaceutically acceptable carriers and excipients comprising 23-25 daily dosage units comprising 250 microgram to 4 mg of drospirenone and 10-20 microgram of ethinyl estrsdiol and 3-5 dosage units comprising 5 to 15 micrograms of ethinyl estradiol, see claim 1 and page 9, lines 15-24 in particular.

Gast (WO 98/04267) does not teach drospirenone or ethinyl estradiol in micronized form.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ drospirenone or ethinyl estradiol in micronized form.

One of ordinary skill in the art would have been motivated to employ known pharmaceutical actives in micronized form because variations of the dosage form of known pharmaceutical actives are considered within the skill of the artisan.

Response to Arguments

Applicant first argues that there is no support for the fact that it would have been obvious to one of ordinary skill in the art to employ drospirenone and ethinyl estradiol in micronized form. Note that intra-conversion of dosage forms of known pharmaceutical agents is within the skill of the Artisan and therefore obvious. Moreover, it is a well-known principle that as the surface area doubles, the volume cubes. Here, micronizing the particles of the active agents increases their surface area, thereby resulting in more dissemination (i.e., surface area increases an order faster as the volume decreases) which would result in increased bioavailability of the actives *in vivo*.

Applicant then refers to the "unexpected results" presented in Example 4. Note that this data is not "clear and convincing." Note that the example shows that absolute bioavailability of orally administered 2 mg of drospirenone is 76%+13%, whereas the absolute bioavailability of microcrystalline suspension 3.13 mg of drospirenone is 85%+24%. Note that the two ranges of absolute bioavailability of drospirenone do overlap. Further note that different amounts of drospirenone were administered, i.e., mg vs. 3.13 mg therefore different bioavailability measurements would have been expected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mojdeh Bahar whose telephone number is (703) 305-1007. The examiner can normally be reached from 8:30 a.m. to 6:30 p.m. Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Mojdeh Bahar
Patent Examiner
April 29, 2002

RUSSELL TRAVERS
PRIMARY EXAMINER
GROUP 1200